Citation:

Johnson L, van Jaarsveld CH, Emmett PM, Rogers IS, Ness AR, Hattersley AT, Timpson NJ, Smith GD, Jebb SA. Dietary energy density affects fat mass in early adolescence and is not modified by GTO variants. *PLoS One*. 2009; 4 (3): 34, 594.

PubMed ID: 19259258

Study Design:

Prospective Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To test the relationship between dietary energy density and fat mass in early adolescence and its interaction with FTO (rs9939609) variants.

Inclusion Criteria:

- This study is part of the *Avon Longitudinal Study of Parents and Children (ALSPAC)* and all pregnant women in Avon with an expected delivery date between April 1, 1999 and December 31, 1992 were eligible for inclusion in the study
- For this analysis, children with available data on genotype, diet and fat mass were included.

Exclusion Criteria:

Children without data on:

- Genotype
- Diet
- Fat mass.

Description of Study Protocol:

Recruitment

None reported; described elsewhere.

Design

Analyses were performed to determine whether a relationship existed between:

- Dietary energy density (DED) and body fatness
- FTO genotype status and body fatness, and to determine whether DED and FTO genotype status interact to influence body fatness in a group of adolescent children who had diet assessed at age 10 years and body composition assessed at age 13 years.

Dietary Intake/Dietary Assessment Methodology

- Dietary data were collected using three-day unweighted diet diaries when children were aged 10.7±0.3 years of age
- Children completed the diary, with parental help and brought it to the clinic where a nutritionist would check the diaries with the child and parents and clarified missing or ambiguous details
- If a diary had not been completed by the child, a single 24-hour recall was administered at the clinic, and this occurred in 13.5% of cases.

Blinding Used

Not applicable.

Intervention

Not applicable.

Statistical Analysis

- Association between two continuous variables were assessed using Pearson's correlation coefficient
- T-tests or ANOVA were used to test for differences in means in two or more groups
- Non-parametric tests Mann Whitney and Kruskall Wallis were used when the assumptions of the T-test or ANOVA were not met
- Chi square tests were done to assess association between two categorical variables or departure of allele frequencies from Hardy Weinberg Equilibrium
- Multiple linear regression analysis was used to model the determinants of fat mass at age 13 years
- Misreporting of energy intake was estimated using an individualized method by calculating the ratio of reported energy intake to estimated energy requirements (EER)
- A power calculation was performed using the program Quanto to estimate the size of the smallest interaction effect detectable in a sample of N=4,318 with a power of 0.8.

Data Collection Summary:

Timing of Measurements

- Dietary data was collected when children were aged 10.7±0.3 years
- Fat mass was measured when children were aged 12.8±0.2 years.

Dependent Variables

- Fat mass (kg) was measured using Dual-energy X-ray Absorptometry (DEXA)
- Fat Mass Index (FMI) was calculated by dividing fat mass (kg) by height (m) in order to adjust for body size

- Height was adjusted so that the relationship between fat mass and height was completely removed.

Independent Variables

- Dietary energy density (kJ/g) (DED) was measured using three-day unweighted food records or a 24-hour recall and was calculated (excluding drinks) by dividing total food energy (kJ) by total food weight (g)
- Genotpying was done to determine FTO status (rs9939609) using florescence based competitive allele-specific PCR.

Control Variables

- Misreporting of energy intake was estimated using an individualized method by calculating the ratio of reported energy intake (EI) to estimated energy requirements (EER)
- Overweight status at baseline [body mass index (BMI)] was used as a covariate to separate a diet associated with high fat mass from a diet associated with later adiposity because of high fatness at baseline
- Puberty was assessed using Tanner stage as reported by parents at age 13 years to control for puberty's effect on body composition and energy needs
- Parental SES and maternal education were self-reported via questionnaires
- TV watching was reported by parents in questionnaires completed at age eight years
- Physical activity was measured over seven days at age 12 using accelerometers.

Description of Actual Data Sample:

- *Initial N:* 14,541 children
- *Attrition (final N):*
    - 4,318 children had data on diet, fat mass and FTO genotype
    - 2,275 children had data on diet, fat mass, FTO genotype and potential confounders
- *Age:* Children were followed from infancy; for these analyses diet data from age 10 years and fat mass data from age 13 years were used
- *Ethnicity:* None reported
- *Other relevant demographics:* None reported
- *Anthropometrics:* None reported
- *Location:* Avon, United Kingdom.

Summary of Results:

- Fat mass index (FMI) at age 13 years was significantly higher among carriers of the high risk A allele. After adjusting for potential confounders, each A allele was associated with 0.35±0.13kg more fat mass at 13 years
- DED at age 10 years was significantly associated with fat mass at age 13 years. After adjusting for potential confounders, each kJ/g increase was associated with 0.16±0.06kg more fat mass at age 13 years
- Carriers of A allele had a higher energy intake (EI) at 10 years, but there was no evidence of interaction between DED and FTO genotypes at age 10 years.

Other Findings

- Mean DED in all children with data on diet at age 10 years was 8.76±1.63kJ/g
- Increased DED at age 10 years was associated with a higher EI (P<0.0001)
- At age 10 years, 63% of children had plausible reported of EI. Under-reporters of EI at age 10 years were more likely than plausible-reports to be defined as overweight at age 10 (42% vs. 12%) and 13 years (47% vs. 19%). Mean DED was lower among under-reporters compared to plausible reporters (8.45±1.67kJ/g vs. 8.87±1.56kJ/g; P<0.0001). In a basic regression model, there was no evidence that fat mass at age 13 years was associated with DED at age 10 years, but after adjusting for reporting accuracy, each kJ/g of DED at age 10 years was associated with 0.21±0.05kg more fat mass at age 13 years
- DED was lower in those children with complete data on all confounders compared to those children with missing data (P<0.001).

Author Conclusion:

The authors drew the following conclusions from these analyses:

- There was no evidence of an interaction between DED and FTO genotype on fat mass (i.e., there was no evidence that the effect of DED on fat mass was altered by the FTO genotype)
- DED at age 10 years and FTO genotype contribute independently to increase fat mass at age 13 years. Each A allele of FTO was associated with 0.35kg more fat mass at 13 years and each 1kJ/g DED at 10 years was associated with 0.16kg more fat mass at 13 years, after controlling for misreporting of energy intake, gender, puberty, maternal education, TV watching, physical activity and overweight status at 10 years
- Because weight status at age 10 years attenuated the effects of both FTO and DED at 10 years on fat mass at 13 years, it is possible that overweight children are more likely to consume more energy dense diets, which supports a causal role for DED in increasing fat mass over time.

Reviewer Comments:

- *The authors used three-day food records as the primary source of dietary data. However, in cases where the three-day food record was not completed, a 24-hour recall was used instead. This occurred in 13.5% of cases. It is unclear what the impact the use of different dietary data collection methods was on results*
- *Dietary, genetic and body composition data was available for only 30% of the subjects enrolled in the ALSPAC study. Results showed that children with complete data had a lower DED compared to those without complete data, which may mean that the effect of DED on fatness was under-estimated.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	N/A

	2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
	3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
	4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	N/A

Validity Questions

1.	**Was the research question clearly stated?**		Yes
	1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
	1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
	1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**		Yes
	2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
	2.2.	Were criteria applied equally to all study groups?	Yes
	2.3.	Were health, demographics, and other characteristics of subjects described?	No
	2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**		Yes
	3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
	3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
	3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	N/A
	3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes

	3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
	3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**		Yes
	4.1.	Were follow-up methods described and the same for all groups?	Yes
	4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
	4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
	4.4.	Were reasons for withdrawals similar across groups?	Yes
	4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**		Yes
	5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	Yes
	5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
	5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	Yes
	5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
	5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**		Yes
	6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
	6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
	6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
	6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes

6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	Yes
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	Yes
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes

9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes